J Gastrointest Surg (2015) 19:955–963
DOI 10.1007/s11605-015-2751-1

REVIEW ARTICLE

Effect of Billroth II or Roux-en-Y Reconstruction for the Gastrojejunostomy After Pancreaticoduodenectomy: Meta-analysis of Randomized Controlled Trials

Ji Yang · Chao Wang · Qiang Huang

Received: 18 October 2014 / Accepted: 8 January 2015 / Published online: 19 March 2015

Abstract
Background and Objectives This study aimed to compare Billroth II with Roux-en-Y reconstruction after pancreaticoduodenectomy (PD).
Methods A literature search was carried out to identify all randomized controlled trials (RCTs) comparing postoperative complications of Billroth II versus Roux-en-Y reconstruction following PD published from 1 January 1990 to 31 August 2014. Pooled risk ratios (RRs) with 95 % confidence intervals (CIs) were calculated using fixed effects or random effects models
Results In total, three RCTs with 470 patients were included. Using International Study Group of Pancreatic Surgery (ISGPS) definitions, incidences of delayed gastric emptying (DGE) [grades B and C (3.9 versus 12.9 %; RR 0.30, 95 % CI 0.11–0.79; P=0.01), DGE grade C (0.7 versus 9.6 %; RR 0.11, 95 % CI 0.02–0.61; P=0.01)] were significantly lower in the Billroth II group than in the Roux-en-Y group, as was the length of hospital stay (weighted mean difference −4.72, 95 % CI −8.91, −0.53; P=0.03).
Conclusions Meta-analysis revealed that the incidence of DGE (grades B and C) after PD can be decreased by using Billroth II rather than Roux-en-Y reconstruction.

Keywords Billroth II reconstruction · Delayed gastric emptying · Gastrojejunostomy · Pancreatic fistula · Pancreaticoduodenectomy · Roux-en-Y reconstruction

Introduction

Pancreaticoduodenectomy (PD) represents the only and adequate surgical option for many malignant and benign diseases of the pancreaticoduodenal area. Although mortality after PD has decreased to fewer than 5 % in high-volume centers, it is still accompanied by a high postoperative complication rate (30–50 %).[1–8] In most series, the three leading causes of morbidity after PD are postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE), and wound infection.[6–9] The leakage of activated pancreatic enzymes with autolytic activity as well as the pancreatic fistula can cause injury to the surrounding intra-abdominal tissues, giving rise to abscesses, sepsis, and life-threatening hemorrhage. So the POPF can be a source of considerable morbidity and may contribute to mortality. The reported POPF rate after PD ranges from 5 to 25 % in most high-volume centers.[1,4–5]

Since the PD was first described by Allen Whipple et al.[10] back in the 1930s, many efforts have been made to reduce the main postoperative complication pancreatic anastomotic leakage after PD, such as the creation of pancreaticogastrostomy (PG) and pancreaticojejunostomy (PJ),[11,12] duct ligature, duct occlusion by synthetic polymers as Ethiblock or Neoprene,[13,14] and the placement of pancreatic duct stents.[15] DGE is also a major postoperative complication after PD and is seen in a significant proportion of patients, contributing to prolong hospital stay and increase in hospital costs.

Ji Yang and Chao Wang contributed equally and are the first authors.

Ji Yang and Chao Wang contributed equally to this work.

J. Yang · C. Wang · Q. Huang (✉)
Department of General Surgery, Hepatobiliary and Pancreatic Laboratory of Anhui Province, Affiliated Provincial Hospital of Anhui Medical University, 17# Lujiang Road, Hefei 230001, China
e-mail: hq_sohu@sohu.com

J. Yang
e-mail: ahslyyyangji@163.com

Although DGE is not a life-threatening morbidity after PD, this condition often results in delaying the oral intake, prolonging the hospital stay, decreasing the life quality of patients after operation, and increasing the cost of hospitalization. DGE is induced by postoperative intra-abdominal complications such as bleeding, ileus, and infection.[16] Due to the disadvantage and influence of DGE, various technical and therapeutic methods have been advocated to decrease the incidence of DGE after PD. These include pyloric dilation,[17] preoperative use of erythromycin,[18] the preservation of the left gastric vein,[19] and the construction of duodenojejunostomy (DJ) or gastrojejunostomy (GJ).[20,21]

There has been long-standing interest in the development of techniques to reduce the rate of POPF, DGE, and its associated morbidity. Studies have reported that the route of DJ or GJ might have a role in decreasing the incidence of POPF and DGE. Also the debate between the Roux-en-Y reconstruction and the Billroth II (B-II) reconstruction still remains controversial. The use of Roux-en-Y or isolated Roux loop reconstruction is a technique which reduces the activation of pancreatic juice by biliary secretion will reduce the incidence of POPF-related morbidity and mortality in patients undergoing PD compared to that of B-II reconstruction.[23] However, in the B-II reconstruction, the gastric passage can more easily and smoothly pass down to the jejunum because of two direct routes to the afferent and efferent jejunum compared with the Roux-en-Y (R-Y) reconstruction. At almost high-volume centers, this type of reconstruction is selected because of the low DGE incidence of Billroth II reconstruction.[24] Currently, studies comparing the Billroth II or Roux-en-Y are small sizes or retroprospective.[25,26] Therefore, it is still controversial as to which is the best reconstruction for reducing the POPF, DGE, and its associated morbidity after PD. Due to the relatively small sample sizes of previous randomized controlled trials (RCTs), it is difficult to draw a definitive conclusion. The present paper is a meta-analysis of all published RCTs performed since 1990. It is an effort to determine the best method of reconstruction after PD.

Material and Methods

Search Strategy

A computerized literature search of the Medline, Embase, Web of Science, Cochrane Library, and Cochrane Clinical Trials Registry databases was performed to identify articles published in English until 31 August 31 2014. The following MeSH terms combined with free-text search terms were used: pancreatic resection, pancreaticoduodenal resection, Whipple's operation, pancreaticoduodenectomy, Roux-en-Y, isolated Roux loop, and Billroth II. The function of "related articles" was used to broaden the search, and all abstracts, studies, and citations scanned were reviewed. Two researchers (J.Y. and C.W.) searched for articles independently.

Inclusion and Exclusion Criteria

This systematic review and meta-analysis were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[27]

Inclusion Criteria

Inclusion criteria include the following: (1) only prospective randomized controlled trials were included in this study; PD procedures performed for any reason (malignant or benign pancreatic tumor, chronic pancreatitis, etc.) were included; (2) all the studies were published in English and compared the Billroth II and Roux-en-Y or isolated Roux loop using the quantitative data on POPF, DGE, and other overall complications; and (3) the study publication of the included studies was from 1 January 1990 to 31 August 2014.

Exclusion Criteria

Exclusion criteria include the following: (1) studies that did not report adequately postoperative complications, reoperations, and mortality were excluded; (2) any studies were excluded if the participants were younger than 18 years; (3) PD without immediate pancreatic anastomosis or duodenum-preserving pancreatectomy was excluded; and (4) observational studies, case reports, and prospective studies were excluded.

Data Extraction and Quality Assessments

Data regarding study description, population characteristics, intraoperative conditions, and outcome parameters were extracted independently by two authors (J.Y. and C.W.). Inconsistencies were resolved by consensus, and when this could not be reached, the third author adjudicated. The quality of all studies was evaluated using the scoring systems of Jadad et al.[28] The Jadad scales were used to evaluate the included articles according to appropriate randomization, double blinding, and adequate description of withdrawals and dropouts.

Statistical Analysis

The statistical analyses were performed using the Review Manager (RevMan) version 5.2.10 software. We analyzed dichotomous variables using estimation of risk ratio (RR) with 95 % confidence interval (CI) and continuous variables using weighted mean difference (WMD) with 95 % CI. $P<0.05$ indicated statistically significant difference. Before performing meta-analyses, homogeneity of effect sizes was assessed using chi-square test to determine the I^2 value. We

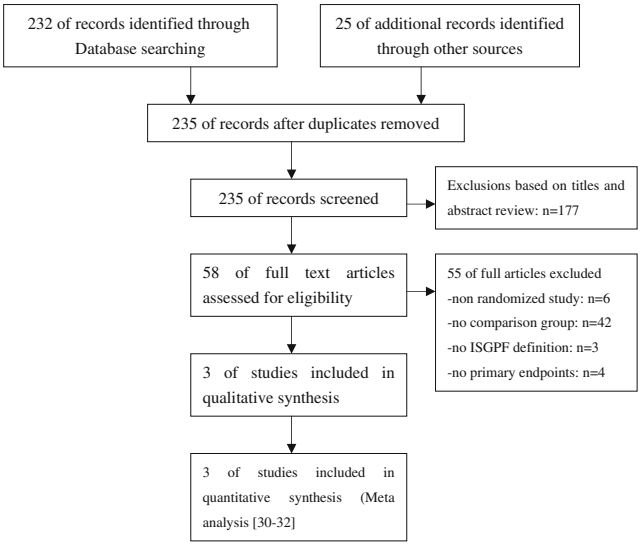

Fig. 1 Study selection conducted in line with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines

considered heterogeneity to be present if the I^2 statistic was >50 %. A fixed effects (Mantel-Haenszel) statistical model was used in the absence of significant heterogeneity. On the other hand, a random effects (DerSimonian and Laird)[29,30] model was used. If the heterogeneity was high or extracted data were less than three sets, we performed subgroup analysis. Publication bias was examined in a funnel plot of log RR against its standard error using Begg's test, and the degree of asymmetry was tested statistically using Egger's unweighted regression asymmetry test

Results

Systematic Search

A total of 257 studies were searched in the databases; after reading the full text and the qualitative synthesis of the 257 articles, finally, three RCTs enrolling a total of 470 patients were included.[31–33] The flow of PRISMA statement of literature selection process is shown in Fig. 1. The two reviewers had 100 % agreement in the reviews of the data extraction.

Description of Included Studies

Baseline patient, study characteristics, and surgical procedures are shown in Tables 1, 2, and 3. A total of 470 patients were included in the study, 237 in the Billroth II group and 233 in the Roux-en-Y group. Two[31,32] of the three studies were single-center study and the other one was multicenter study.[33] There were no differences between groups in the patient's age and sex or the pathology that motivated PD in all included studies. Pancreatic cancer was the most frequent diagnosis, followed by other tumors of the pancreaticoduodenal area.

Quality Assessment of the Included Studies

According to the Jadad et al., two of the studies[31,33] included were of low quality as a result of their use of inadequate randomization methods (randomized during the operation) and the absence of blinding, power calculations, and intention-to-treat analysis. The other trial[32] was scored as being of high strength as a result of their use of relatively good randomization techniques and the presence of blinding, power calculations, and intention-to-treat analysis. The score of the included studies were 4 points of Tani et al.[31] and Ke et al.[33] and 5 points of Shimoda et al.[32] (Table 4)

Outcomes of Interests

The primary outcomes of the present meta-analysis was the incidence of DGE which includes grades A, B, and C. The definition of DGE was proposed by the International Study Group of Pancreatic Surgery (ISGPS).[35] DGE was classified into three grades based on its clinical impact: grade A, need for nasogastric tube (NGT) intubation for 4 days or NGT reinsertion after postoperative day (POD) 3 or inability to tolerate a solid diet by POD 7; grade B, need for NGT intubation for 8 days or NGT reinsertion after POD 7 or inability to tolerate a solid diet by POD 14; and grade C, need for NGT

Table 1 Populations and clinical characteristics of the included studies

Study	Year	Patients		Age (years)	Gender (M/F)	Study period
		Groups	Numbers			
Tani M et al.[31]	2014	Billroth II	76	68.0±8.9	42/34	June 2009–September 2012
		Roux-en-Y	77	69.6±7.9	39/36	
Shimoda et al.[32]	2013	Billroth II	52	66.5±9.8	20/32	April 2008–August 2011
		Roux-en-Y	49	65.7±11.1	21/28	
Ke et al.[33]	2013	Billroth II	109	59.3±6.6	50/59	January 2006–April 2012
		Roux-en-Y	107	58.3±5.9	51/56	

Table 2 Pathologies and surgical procedures of the included studies

Study	Year	Groups	Pathologies						Operation type	Surgical techniques	Stenting
			PC	BC	DC	AC	OT	CP			
Tani et al.[31]	2014	Billroth II	37	11	2	6	18	2	Pylorus-resecting PD	End-to-side hepaticojejunostomy and GJ	Yes
		Roux-en-Y	38	11	2	7	14	3	Pylorus-resecting PD	End-to-side PJ	Yes
Shimoda et al.[32]	2013	Billroth II	46					6	SSPPD	End-to-side GJ Duct-to-mucosa PJ; 2 layers	Yes
		Roux-en-Y	44					5	SSPPD	End-to-side GJ Duct-to-mucosa PJ; 2 layers	Yes
Ke et al.[33]	2013	Billroth II	39	32	6	18	12	0	Standard PD	End to side Duct to mucosa; 2 layers	Yes
		Roux-en-Y	37	35	8	16	13	0	Standard PD	End to side Duct to mucosa; 2 layers	Yes

PC pancreatic cancer, *BC* biliary cancer, *DC* duodenal cancer, *AC* ampullary cancer, *OT* other tumors, *CP* chronic pancreatitis, *SSPPD* subtotal stomach-preserving pancreaticoduodenectomy, *PJ* pancreaticojejunostomy, *GJ* gastrojejunostomy

intubation for 15 days or NGT reinsertion after POD 14 or inability to tolerate a solid diet by POD 21, based on the ISGP S definition. DGE grade B/C was clinically important because it prolonged the hospital stay after PD and increased the hospital cost. The secondary outcome of the present study was POPF. Definitions of pancreatic fistula and its severity were extracted from the International Study Group on Pancreatic Fistula (ISGPF)[34] in the three included RCTs. In the ISGPF definition, POPF was classified as grade A, B, or C and grade B fistulas. Grade C POPF is a severe, clinically significant fistula that requires major deviations in clinical management. The other outcome measures included intra-abdominal abscess, bile leak, postoperative length of stay (LOS), peptic ulcer, wound infection, postoperative pneumonia, reoperation, morbidity, and mortality.

Primary Outcome: DGE

The meta-analysis of the primary outcome investigated the occurrence of DGE (grades A, B, and C) in all of the included RCTs (18.1 %). Meta-analysis indicated that there was no significant difference in DGE (grades A, B, and C) between the Billroth II and Roux-en-Y groups (fixed effects model, 16.4 versus 19.9 %; RR 0.83, 95 % CI 0.56–1.21; P=0.34) (Fig. 2). In the subgroup analysis of the occurrence of DGE (grades B and C), the meta-analysis indicated that the Roux-en-Y reconstruction group had a significantly higher rate of DGE (grades B and C) compared to Billroth II (3.9 versus 12.9 %; relative risk 0.30, 95 % CI 0.11–0.79; P=0.01) (Fig. 3). The subgroup analysis also indicated that DGE grade C was less likely to occur in Billroth II group (0.7 versus 9.6 %; RR 0.11, 95 % CI 0.02–0.61; P=0.01).

Secondary Outcomes

POPF

All trials included provided specific information about total POPF rate in the two groups, but not classified into the three grades (A, B, and C). There was no significant heterogeneity

Table 3 Definition of the postoperative complications in the included studies

Study	Year	Primary objective	Secondary objective	Inclusion criteria	Definition of pancreatic fistula	Definition of DGE
Tani et al.[31]	2014	Pancreatic fistula within 30 days of operation	Mortality and complications within 30 days of operation	Benign or malignant tumor in the pancreatic periampullary region	According to the ISGPF[34] definition	According to the ISGPS[35] definition
Shimoda et al.[32]	2013	Delayed gastric emptying (DGE)	Pancreatic fistula Mortality Postoperative length of stay	Benign or malignant tumor in the pancreatic periampullary region	According to the ISGPF[34] definition	According to the ISGPS[35] definition
Ke et al.[33]	2013	POPF	Postoperative complications Postoperative hospital stay	Benign or malignant tumor in the pancreatic periampullary region	According to the ISGPF[34] definition	According to the ISGPS[35] definition

ISGPF International Study Group on Pancreatic Fistula, *ISGPS* International Study Group of Pancreatic Surgery, *POPF* postoperative pancreatic fistula

Table 4 Quality assessment of the included studies

Study	Year	Centers	Randomized	Double blinding	Description of withdraws and dropouts	Total scores
Tani et al.[31]	2014	Single center	During the operation	Yes	Yes	4 points
Shimoda et al.[32]	2013	Single center	Before the operation	Yes	Yes	5 points
Ke et al.[33]	2013	Multicenter	During the operation	Yes	Yes	4 points

among these trials (I^2=1 %; P=0.37). Meta-analysis showed that the occurrence of POPF was statistically similar in both groups (24.4 versus 20.7 %; RR 1.25, 95 % CI 0.80–1.96; P=0.32) (Fig. 4).

Postoperative LOS

Two trials[31,32] that included 252 patients reported the data of postoperative length of stay. Meta-analysis showed that the postoperative LOS was significantly shorter in the Billroth II group than in the Roux-en-Y group (fixed effects model, WMD −4.72, 95 % CI −8.91, −0.53; P=0.03). However, significant heterogeneity was apparent among the two trial studies (I^2=64 %; P=0.10) (Table 5).

Operation Time

All trials included provided the data of operation time between the groups. Meta-analysis showed that the operation time was significantly shorter in the Billroth II group than in the Roux-en-Y group (fixed effects model, WMD −6.60, 95 % CI −12.72, −0.49; P=0.03). There was no significant heterogeneity among these trials (I^2=19 %; P=0.29).

Bile Leak

Two trials[31,33] compared Billroth II with Roux-en-Y for the occurrence of bile leak. Using a fixed effects model, the pooled data showed that there was no significant difference in postoperative bile leak between the two groups (2.7 versus 1.6 %; RR 1.64, 95 % CI 0.40, 6.76; P=0.49) and no significant heterogeneity (I^2=0 %; P=0.85) (Table 5).

Intra-abdominal Abscess

Intra-abdominal abscess was analyzed in the two studies.[31,33] Rates of intra-abdominal abscess in the Billroth II and Roux-en-Y groups were 7.6 and 5.9 %, respectively, and thus showed no significant difference (RR 1.27, 95 % CI 0.60, 2.70; P=0.54). No heterogeneity was found (I^2=0 %; P=0.70).

Peptic Ulcer

Postoperative peptic ulcer occurrence was similar between groups from the pooled analysis (fixed effects model, RR 0.33, 95 % CI 0.04, 3.18; P=0.34) from two RCTs.[31,33] Also no heterogeneity was found (I^2=0 %; P=0.99).

Wound Infection

The rate of postoperative wound infection was similar between the two groups. The data from two RCTs[31,33] was amenable for pooling showing a RR of 1.31 (95 % CI 0.78, 2.19; P=0.30). No statistical heterogeneity was found (I^2=0 %; P=0.40).

Pneumonia

At last, the occurrence of postoperative pneumonia was similar between the two groups. The pooled data from two RCTs[31,33] showed a RR of 0.98 (95 % CI 0.35, 2.74; P=0.97) with the fixed effects model. No statistical heterogeneity was found (I^2=0 %; P=0.51).

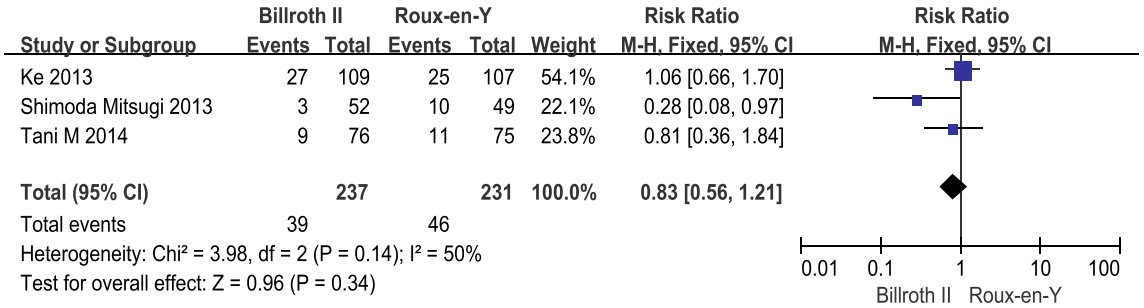

Fig. 2 Comparison of Billroth II versus Roux-en-Y in terms of DGE (grades A, B, and C)

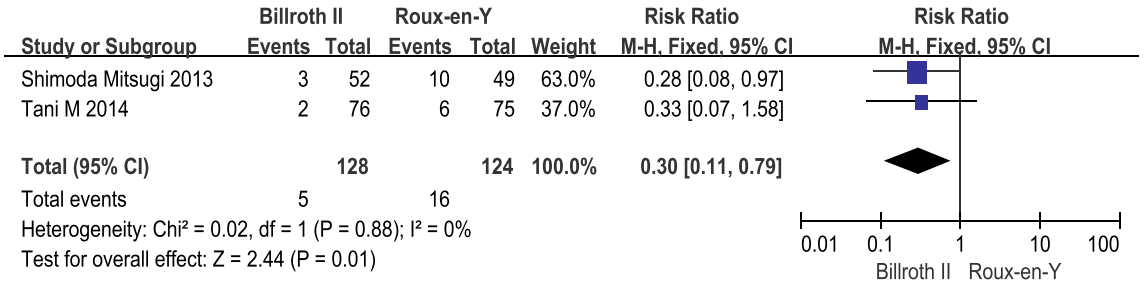

Fig. 3 Comparison of Billroth II versus Roux-en-Y in terms of DGE (grades B and C)

Publication Bias

To explore the publication bias in the present meta-analysis, a funnel plot analysis (Fig. 5) was applied to assess the possibility of publication bias; findings showed a nonsignificant likelihood.

Discussion

Since the PD was first described by Allen Whipple et al.[10] back in the 1930s, the best technique for pancreatic anastomosis has remained controversial. The present meta-analysis and systemic reviews of three RCTs allowed for an analysis of pooled data for Roux-en-Y and Billroth II reconstruction, respectively, after PD. Also the present study was the first meta-analysis which compared the Roux-en-Y and Billroth II reconstruction after the PD. The pooled results showed that the Billroth II reconstruction represents a better option than Roux-en-Y reconstruction by comparing the occurrences of DGE (grades B and C), DGE grade C, and postoperative length of hospital stay. However, no differences between the groups emerged in terms of pancreatic fistula, bile leak, intra-abdominal abscess, peptic ulcer, wound infection, and pneumonia.

Many studies have reported the incidence and the risks of DGE when it was first reported by Warshaw[36] after PPPD. Up to now, the precise mechanism of DGE has not yet been clarified. DGE is thought to be caused by various risk factors, such as the age of patient, pylorospasm caused by disruption of the vagal nerve system and vascular supply to the antropyloric region, angulation or torsion of the DJ,[37] and other postoperative morbidities such as PF and intra-abdominal abscess. Various studies including resection and reconstruction methods and postoperative medication with erythromycin have been performed to decrease the occurrence of DGE.[6] In this study, we compared the incidence of DGE, POPF, and other complications after PD in Billroth II versus Roux-en-Y reconstruction through the systemic review and meta-analysis, and we found that Billroth II reconstruction was associated with a decrease incidence of DGE (grades B and C) after PD (3.9 versus 12.9 %; relative risk 0.30, 95 % CI 0.11–0.79, P=0.01). According to the ISGPS classification of DGE, DGE (grades B and C) was clinically important because it prolonged the hospital stays after PD and can increased the hospital cost. The decrease of DGE in Billroth II mainly because of the gastric passage can more easily and smoothly pass down to the jejunum because of two direct routes to the afferent and efferent jejunum compared with the Roux-en-Y (R-Y) reconstruction. The present meta-analysis concluded that the Billroth II had a shorter operation time than that of Roux-en-Y reconstruction (fixed effects model, WMD −6.60, 95 % CI −12.72, −0.49; P=0.03). Also the present meta-analysis revealed a result that the Billroth II reconstruction was associated with shorter hospital stays after the PD than that of Roux-en-Y procedures (fixed effects model, WMD −4.72, 95 % CI −8.91, −0.53; P=0.03).

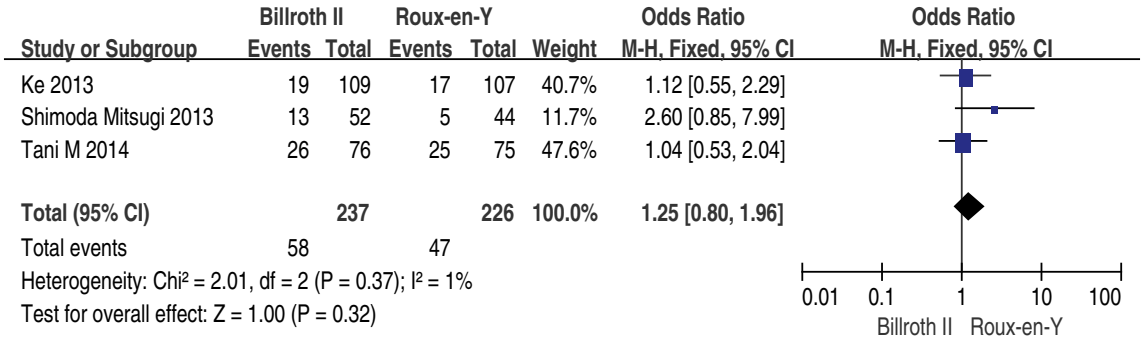

Fig. 4 Comparison of Billroth II versus Roux-en-Y in terms of POPF

Table 5 Meta-analysis results of the outcomes

Outcomes	Included studies	Heterogeneity		RR/WMD	
		I^2 (%)	*P*	95 % CI	*P*
DGE (all grades)	30–32	50	0.14	0.83 (0.56, 1.21)	0.34
DGE (grade B)	30–31	0	0.97	0.96 (0.25, 3.77)	0.96
DGE (grade C)	30–31	0	0.97	0.11 (0.02, 0.61)	0.01
DGE (grades B and C)	30–31	0	0.88	0.30 (0.11, 0.79)	0.01
POPF	30–32	1	0.37	1.25 (0.80, 1.96)	0.32
LOS	30–31	64	0.10	−4.72 (−8.91,–0.53)	0.03
Operation time	30–32	19	0.29	−6.60 (−12.72,–0.49)	0.03
Bile leak	30, 32	0	0.85	1.64 (0.40, 6.76)	0.49
Intra-abdominal abscess	30, 32	0	0.70	1.27 (0.60, 2.70)	0.54
Peptic ulcer	30, 32	0	0.99	0.33 (0.04, 3.18)	0.34
Wound infection	30, 32	0	0.40	1.31 (0.78, 2.19)	0.30
Pneumonia	30, 32	0	0.51	0.98 (0.35, 2.74)	0.97

Numbers of studies have been demonstrated the pros and cons of the Billroth II versus the Roux-en-Y procedures of PD, of which the most primary endpoints were the incidence of pancreatic fistula. The present meta-analysis showed that the occurrence of POPF was statistically similar in both groups (24.4 versus 20.7 %; relative risk 1.25, 95 % CI 0.80–1.96, P=0.32), which indicates that the Roux-en-Y procedure or the isolated Roux loop does not decrease the incidence of pancreatic anastomotic leakage after PD compared to the Billroth II or conventional reconstruction. As it is known to all, pancreatic fistula is the most important postoperative complication and is at times fatal; it may also play a central role in the development of other intra-abdominal complications, such as hemorrhage and leak. Pancreatic surgeons generally agreed that pancreatic fistula represents the "Achilles heel" of PD.[38,39] Several factors can lead to pancreatic fistula, including disease factors (pancreatic texture, pancreatic pathology, pancreatic duct size, and pancreatic juice output), patient-related factors (age, sex, jaundice, comorbid illness, and previous gastric surgery), surgeon-related factors (familiarity), and operative factors (operation time, type of anastomosis, and stenting of pancreatic duct).[39–42] In the discussion of Billroth II versus the Roux-en-Y procedures in the present meta-analysis, the occurrence of pancreatic fistula was statistically similar. However, based on previous studies,[43–44] we concluded that the Roux-en-Y procedure had several advantages: firstly, isolation of the pancreatic anastomosis from the biliary and gastric anastomoses prevents activation of the secreted inactive precursor pancreatic enzymes by low gastric pH or duodenal enterokinase, and secondly, suction drains placed within the lesser sac adjacent to the pancreatic stump isolate any drainage from around the pancreaticojejunal anastomosis from the rest of the operative field. However, the disadvantages of the Roux-en-Y procedure were the longer operation time, the need for an additional anastomosis, and so on. The Roux-en-Y reconstruction has several advantages which may decrease the pancreatic fistula than that of the Billroth II reconstruction, but in the present meta-analysis,

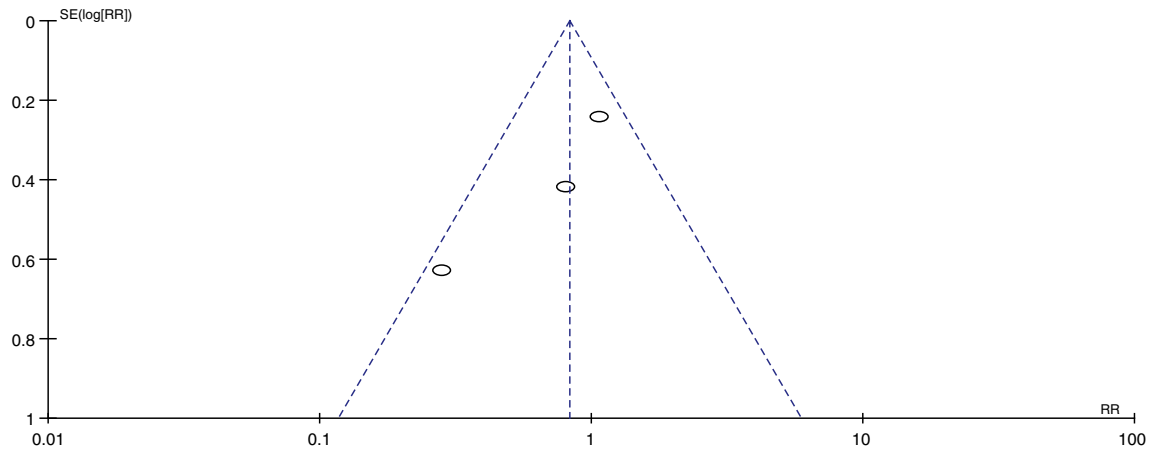

Fig. 5 Funnel plot analysis showing no publication bias for the occurrence of delayed gastric empty. *SE* standard error, *OR* odds ratio

we concluded that the difference of pancreatic fistula was not significant; this was mainly because both Billroth II and Roux-en-Y had the same pancreaticojejunostomy anastomosis in the included studies. On the other hand, the Roux-en-Y procedure was more complicated (an additional anastomosis) and need more time, so that in the clinical practice, the Billroth II procedure is widely used. Hence, in the future, randomized controlled trials are required to further clarify its efficacy.

We also evaluated the incidence of bile leak (biliary fistula), intra-abdominal abscess, peptic ulcer, wound infection, and pneumonia between the two groups. Pooled analysis showed that there exist no statically differences in terms of bile leak, intra-abdominal abscess, peptic ulcer, wound infection, and pneumonia in the Billroth II and Roux-en-Y reconstruction.

However, as an observational study, the limitations of the present meta-analysis should be recognized. At first, the small number of included studies may not provide the comprehensive and precise results, but the present study was the first meta-analysis of randomized controlled trials, the results of the meta-analysis depends on large numbers of the patients in the three included RCTs, and the results were convincing. Secondly, there was clinical heterogeneity in some outcomes, such as the length of hospital stay and the presence of DGE (grades A, B, and C). The heterogeneity was due to the differences in operative technique, the experience of the surgeons, the postoperative management, and so on. For example, the differences of surgical techniques (duct-to-mucosa, invagination, and single-layer, and two-layer methods) may lead to different operation time periods and blood loss, and these factors were risks of the postoperative morbidities and mortality. Thirdly, there were insufficient data for a pooled analysis of the POPF (grade B or C), which cannot provide the sufficient data for comparing the POPF (grades B and C) (clinically, pancreatic fistula). Finally, none of the studies described long-term follow-ups of postoperative mortality and morbidity of the patients after PD, which are crucial to any assessment of the curative effects of Billroth II and Roux-en-Y reconstruction.

In summary, the present study is the first meta-analysis of randomized prospective clinical trials to have demonstrated the superiority of Billroth II over Roux-en-Y in terms of the development of DGE after PD. The incidence of DGE (grades B and C) in the Billroth II group was obviously lower than that in the Roux-en-Y group. Billroth II reconstruction thus seems to have certain benefits in terms of reducing the incidence of severe DGE. Further, adequately powered and well-designed RCTs are required to verify the result and to confirm whether this result can be applied to an equal extent in all patient subgroups.

References

1. Cameron JL, Riall TS, Coleman J, et al. One thousand consecutive pancreaticoduodenectomies. Ann Surg, 2006,244:10–15.
2. Arnaud JP, Tuech JJ, Cervi C, et al. Pancreaticogastrostomy compared with pancreaticojejunostomy after pancreaticoduodenectomy. Eur J Surg, 1999, 165:357
3. Addeo P, Delpero JR, Paye F, Oussoultzoglou E, Fuchshuber PR, Sauvanet A, Sa Cunha A, Le Treut YP, Adham M, Mabrut JY, Chiche L, Bachellier P. Pancreatic fistula after a pancreaticoduodenectomy for ductal adenocarcinoma and its association with morbidity: a multicentre study of the French Surgical Association. HPB 2014;16:46–55.
4. Muscari F, Suc B, Kirzin S, Hay JM, Fourtanier G, Fingerhut A, Sastre B, Chipponi J, Fagniez PL, Radovanovic A. Risk factors for mortality and intra-abdominal complications after pancreatoduodenectomy: multivariate analysis in 300 patients. Surgery 2006; 139:591–8.
5. Winter JM, Cameron JL, Campbell KA, Arnold MA, Chang DC, Coleman J, Hodgin MB, et al. 1423 pancreaticoduodenectomies for pancreatic cancer: a single-institution experience. J Gastrointest Surg 2006; 10:1199–210.
6. Yeo CJ, Cameron JL, Sohn TA, Lillemoe KD, Pitt HA, Talamini MA, et al. Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications, and outcomes. Ann Surg 1997; 226:248–57.
7. Gooiker GA, van Gijn W, Wouters MW, Post PN, van de Velde CJ, et al. Systematic review and meta-analysis of the volume–outcome relationship in pancreatic surgery. Br J Surg 2011; 98: 485–494.
8. Kawai M, Tani M, Terasawa H, Ina S, Hirono S, Nishioka R et al. Early removal of prophylactic drains reduces the risk of intra-abdominal infections in patients with pancreatic head resection: prospective study for 104 consecutive patients. Ann Surg 2006; 244: 1–7.
9. Grobmyer SR, Pieracci FM, Allen PJ, Brennan MF, Jaques DP. Defining morbidity after pancreaticoduodenectomy: use of a prospective complication grading system. J Am Coll Surg 2007; 204: 356–64
10. Whipple AO, Parsons WB, Mullins CR. Treatment of carcinoma of the ampulla of Vater. Ann Surg 1935; 102: 763–779
11. Wente MN, Shrikhande SV, Müller MW, Diener MK, Seiler CM, Friess H et al. Pancreaticojejunostomy versus pancreaticogastrostomy: systematic review and meta-analysis. Am J Surg 2007; 193: 171–183.
12. Topal B, Fieuws S, Aerts R, Weerts J, Feryn T, Roeyen G et al.; Belgian Section of Hepatobiliary and Pancreatic Surgery. Pancreaticojejunostomy versus pancreaticogastrostomy reconstruction after pancreaticoduodenectomy for pancreatic or periampullary tumours: a multicentre randomised trial. Lancet Oncol 2013; 14: 655–662.
13. Madiba TE, Thomson SR: Restoration of continuity following pancreatoduodenectomy. Br J Surg 1995; 82:158–165.
14. Sikora SS, Posner MC: Management of pancreatic stump following pancreaticoduodenectomy. Br J Surg 1995;82:1590–1597
15. Xiong JJ, Altaf K, Mukherjee R, HuangW, HuWM, Li A et al. Systematic review and meta-analysis of outcomes after intraoperative pancreatic duct stent placement during pancreaticoduodenectomy. Br J Surg 2012; 99: 1050–1061
16. Sakamoto Y, Yamamoto Y, Hata S, et al. Analysis of risk factors for delayed gastric emptying (DGE) after 387 pancreaticoduodenectomies with usage of 70 stapled reconstructions. J Gastrointest Surg. 2011; 15: 1789–1797.
17. Fischer CP, Hong JC. Method of pyloric reconstruction and impact upon delayed gastric emptying and hospital stay after pylorus-

preserving pancreaticoduodenectomy. J Gastrointest Surg. 2006; 10: 215–219.
18. Yeo CJ, Barry MK, Sauter PK, et al. Erythromycin accelerates gastric emptying after pancreaticoduodenectomy. A prospective, randomized, placebo controlled trial. Ann Surg. 1993; 218:229–237; discussion 237–238.
19. Kurosaki I, Hatakeyama K. Preservation of the left gastric vein in delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy. J Gastrointest Surg. 2005; 9:846–852.
20. Tani M, Terasawa H, Kawai M, et al. Improvement of delayed gastric emptying in pylorus-preserving pancreaticoduodenectomy: results of a prospective, randomized, controlled trial. Ann Surg. 2006; 243: 316–320.
21. Kurahara H, Shinchi H, Maemura K, et al. Delayed Gastric Emptying after pancreatoduodenectomy. J Surg Res. 2011; 171:e187–192
22. SR. Grobmyer, ST Hollenbeck, DP Jaques et al., Roux-en-Y Reconstruction After Pancreaticoduodenectomy, Arch Surg. 2008;143(12):1184–1188
23. Kawamoto M, Konomi H, Kobayashi K, et al. Type of gastrointestinal reconstruction affects postoperative recovery after pancreatic head resection. J Hepatobiliary Pancreat Surg. 2006; 13:336–343
24. Ballas K, Symeonidis N, Rafailidis S, Pavlidis T, Marakis G, Mavroudis N et al. Use of isolated Roux loop for pancreaticojejunostomy reconstruction after pancreaticoduodenectomy. World J Gastroenterol, 2010, 16:3178–3182.
25. Wayne MG, Jorge IA, Cooperman AM. Alternative reconstruction after pancreaticoduodenectomy. World J Surg Oncol, 2008, 6:9.
26. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009) Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med, 2009, 6(7):1–6
27. Adad AR, Moore RA, Carrol D, Jenkinson C, Reynolds DJ, Gavaghan DJ et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials, 1996, 17:1–12
28. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986; 7: 177–188.
29. Laird NM, Mosteller F. Some statistical methods for combining experimental results. Int J Technol Assess Health Care 1990; 6: 5–30
30. M. Tani, M. Kawai, S. Hirono, K.-I. Okada, M. Miyazawa, A. Shimizu, Y. Kitahata and H. Yamaue, Randomized clinical trial of isolated Roux-en-Y versus conventional reconstruction after pancreaticoduodenectomy, Br J Surg. 2014;101:1084–1091
31. Mitsugi Shimoda, Keiichi Kubota, Masato Katoh, Junji Kita. Effect of Billroth II or Roux-en-Y Reconstruction for the Gastrojejunostomy on Delayed Gastric Emptying After Pancreaticoduodenectomy: A Randomized Controlled Study, Ann Surg 2013;257: 938–942
32. Ke S, Ding XM, Gao J, Zhao AM, Deng GY, Ma RL et al. A prospective, randomized trial of Roux-en-Y reconstruction with isolated pancreatic drainage versus conventional loop reconstruction after pancreaticoduodenectomy. Surgery 2013; 153: 743–752.
33. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, Neoptolemos J, Sarr M, Traverso W, Buchler M. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery 2005; 138:8–13.
34. Wente MN, Bassi C, Dervenis C, et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery. 2007; 142:761–768.
35. Warshaw AL, Torchiana DL. Delayed gastric emptying after pylorus preserving pancreaticoduodenectomy. Surg Gynecol Obstet. 1985; 160:1–4.
36. Itani KM, Coleman RE, Meyers WC, et al. Pylorus-preserving pancreatoduodenectomy. A clinical and physiologic appraisal. Ann Surg. 1986;204:655–664.
37. Haddad LB, Scatton O, Randone B, Andraus W, Massault PP, Dousset B et al. Pancreatic fistula after pancreaticoduodenectomy: the conservative treatment of choice. HPB, 2009, 11:203–209.
38. Reid-Lombardo KM, Farnell MB, Crippa S, Barnett M, Maupin G, Bassi C et al. Pancreatic anastomotic leakage after pancreaticoduodenectomy in 1507 patients: a report from the pancreatic anastomotic leak study group. J Gastrointest Surg, 2007, 11: 1451–1458.
39. Ramacciato G, Mercantini P, Petrucciani N, Nigri GR, Kazemi A, Muroni M et al. Risk factors of pancreatic fistula after pancreaticoduodenectomy: a collective review. ,2011, Am Surg 77: 257–269.
40. Sugimoto M, Takahashi S, Gotohda N, Kato Y, Kinoshita T, Shibasaki H et al. Schematic pancreatic configuration: a risk assessment for postoperative pancreatic fistula after pancreaticoduodenectomy. J Gastrointest Surg, 2013, 7: 1744–1751.
41. Wang Q, He XR, Tian JH, Yang KH. Pancreatic duct stents at pancreaticoduodenectomy: a meta-analysis. Dis Surg, 2013, 30: 415–424.
42. Funovics JM, Zoch G, Wenzl E, Schulz F. Progress in reconstruction after resection of the head of the pancreas. Surg Gynecol Obstet 1987; 164:545–8.
43. Oneil Machado N. Pancreatic fistula after pancreatectomy: definitions, risk factors, preventive measures, and management review. Int J Surg Oncol 2012; 2012:602478.
44. Tolin RD, Malmud LS, Stelzer F, Menin R, Makler PT Jr, Applegate G, et al. Enterogastric reflux in normal subjects and patients with Bilroth II gastroenterostomy. Measurement of enterogastric reflux. Gastroenterology 1979; 77: 1027–33.